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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,935	05/03/2001	David F. Woodward	D2914	6555

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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 11/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/847,935	WOODWARD ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *60-66,68,72,73 and 77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60-66,68,72,73 and 77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *08/26/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of IDS, amendment and remarks filed 08/26/05. Claims 60-66, 68, 72, 73 and 77 are pending.

1. Claims 60-66, 68, 72, 73, 76 and 77 were indicated as allowable. However, upon further consideration, the indicated allowability of these claims is withdrawn in view of the rejections below following.

2. The rejection of claims 78-86 under 35 U.S.C. 102(e) as being anticipated by Gill et al. (US 6,294,553) is withdrawn in light of the cancellation of the claims.

Claim Rejections - 35 USC § 103

3. The rejection of claims 36, 39-41, 43, 44, 47-50, 53-59, 70, 71, 74 and 75 under 35 U.S.C. 103(a) as being unpatentable over Shashoua et al. (US 5,795,909) is withdrawn in light of cancellation of those claims.

4. The rejection of claims 36, 39-41, 43, 44, 47-50, 53-59, 70, 71 and 79 under 35 U.S.C. 103(a) as being unpatentable over Olejnik et al. (US 6,627,210) is withdrawn in light of the cancellation of said claims.

5. The rejection of claims 36, 39, 45-50 and 53-59 under 35 U.S.C. 103(a) as being unpatentable over Hanssler et al. (Derwent Database on West, DE 3309765) is withdrawn in light of the cancellation of said claims.

The rejections below are based on applicants' claim (claim 60) to composition comprising ion-pair complex comprising a therapeutic component that is adrenergic agonist,

efficacy enhancing component and a carrier component, which includes saline. The efficacy enhancing component is selected form fatty acid, anionic polymers and mixtures thereof. The efficacy enhancing component "being effective to enhance the movement of the therapeutic component across a lipid membrane, or biological membrane under physiological conditions" is a property/function of the efficacy enhancing component and a property/function of a product/material or the efficacy enhancing agents is an inherent feature of the product/material or efficacy enhancing component. An ion-pair complex forms between pairs of ions having opposite charge. As is taught in applicants' specification at paragraph 77 of the published application, a complex forms when efficacy-enhancing component is added to a solution containing a therapeutic agent. Thus a solution containing therapeutic component and efficacy enhancing component would have complex formed between the efficacy enhancing component and the therapeutic component.

Claim Rejections - 35 USC § 102

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. Claims 60-63, 65, 66 and 68 are rejected under 35 U.S.C. 102(b) as being anticipated by DeSantis, Jr. et al. (US 5,811,443).

DeSantis discloses combination of at least one clonidine derivative, which is an alpha-2-adrenergic agonist, at least one prostaglandin (abstract; column 2, lines 25-37); the composition may additionally contain anionic mucomimetic polymers in amounts of between about 0.05 and about 8.0 wt% and specifically pourable liquid formulations contain between about 0.05 and 2.0

wt % (column 8, lines 57-64) of the anionic polymers; the composition further comprises agents for adjusting tonicity and osmolality and those agents include sodium chloride, potassium chloride, mannitol, dextrose, glycerine and propylene glycol (column 8, lines 32-36) and the tonicity agents are used in amounts of between about 0.1 to about 10.0 wt% (column 8, lines 36-38). The composition is aqueous and has pH of between 3.5 and 8.0 and osmolality of between 280 to 320 milliOsmoles per kilogram (column 9, lines 35-37).

Prostaglandin is physiologically active compound derived from fatty acid. The anionic polymer is the efficacy-enhancing component. A solution of sodium chloride and water is saline and meets the limitation of saline in claim 1. Since according the applicants' specification, a complex forms between the therapeutic component and the efficacy-enhancing component in solution, it is plausible that a complex is formed between the clonidine, which is the therapeutic component and the anionic polymer, which is the efficacy-enhancing component.

The upper limit amount of the ionic polymer of about 2 wt% of the prior art lies within the efficacy enhancing polymer ranging in amounts of greater that 0.2% and less than 10%, the 2 wt% is less than 10%. Clonidine is alpha-2-adrenergic agonist. A pH of about 8 is greater that about 7 and lies between about 7 and about 9 and DeSantis thus meets the limitations of claims 65 and 66. While the recitation of claim 68 could be a property of the formulation or the intended use of the formulation, it is noted that the composition of DeSantis is suitable for topical ophthalmic application (see claim 6).

Therefore, DeSantis meets the limitations of the designated claims.

8. Claims 60-63, 65, 66, 68, 72 and 73 are rejected under 35 U.S.C. 102(e) as being anticipated by Beck et al. (US 6,358,935).

Beck discloses composition comprising brimonidine (0.2% w/v), sodium carboxymethylcellulose (0.5%) and cyclodextrin (present in Example 2); the composition is at pH of 7.4 (Examples 1 and 2) and in saline (column 6, line 59). pH of 7.4 is greater than 7 and lies between the recited pH of 7-9 (claims 65 and 66). Specifically, Beck discloses the formation of complex between cyclodextrin and the therapeutic agent (column 6, lines 18-40). The carboxymethylcellulose meets the limitation of an additional efficacy-enhancing component of claim 77.

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claim Rejections - 35 USC § 103

9. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

10. Claims 60-63, 65, 66, 72, 73 and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gil et al. (US 6,294,553).

Gil discloses a composition that comprises brimonidine, which is a 5-bromo-6 (2-imidazolin-2-ylamino) quinoxaline and an alpha-2-agonist (abstract, column 2, lines 50 and 61,column 3, lines 12, and 37-39), oleic acid or anionic surfactant (column 4, lines 20-22), buffers (column 4, lines 28-37), physiological saline solution and vehicles such as poloxamers

and cellulose polymers (column 4, lines 4-10); the composition of Gil is applicable as an ophthalmic with a physiological saline solution as the vehicle and where the pH of the ophthalmic composition is between 6.5 and 7.2 (column 3, lines 65-67). Oleic acid is a fatty acid. Effective amount is any amount. A pH of 7.2 is greater than 7 and lies between 7 and 9 (claims 65 and 66). Oleic acid and anionic polymers are efficacy-enhancing components. Oleic acid is a fatty acid.

Gill does not disclose the amount of the efficacy-enhancing component. However, differences in concentration/amounts will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration/amount is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Secondly, there is no demonstration in applicants' specification showing that efficacy enhancing component in amounts greater than 0.2% and less than 10% provides unusual results. Also, since Gillis silent on the amount of the efficacy-enhancing component, it would appear that all or certain amount of the efficacy-enhancing component would be suitable to provide the desired effect and it is within the purview of the person of skill or of ordinary skill to determine the workable amount of the efficacy-enhancing component. The burden is on applicants to demonstrate such is the case.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the quinoxaline composition according to Gill. One having ordinary skill in the art at the time the invention was made to use amount of efficacy enhancing

component effective for ocular composition. "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2). The difference between the prior art and the claims is the amount of the efficacy-enhancing component. Generally, differences in concentration/amounts will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration/amount is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105

USPQ 233, 235 (CCPA 1955). The amounts of the efficacy enhancing components do not patentably distinguish the claimed invention over the prior art absent factual evidence.

11. Claims 60-63, 65, 66 and 68 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over DeSantis, Jr. et al. (US 5,811,443).

The anticipatory rejection is described above. However, the amount of the efficacy-enhancing component is encompassed within the recited range. It would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the composition of DeSantis with about 0.05 and 2.0 wt % efficacy-enhancing component. One having ordinary skill in the art would have been motivated to use an amount desired to provide the ocular composition. The upper limit intersects a point in the recited range for the efficacy-enhancing component.

12. Claims 64 is rejected under 35 U.S.C. 103(a) as being unpatentable over DeSantis, Jr. et al. (US 5,811,443).

DeSantis is discussed above. DeSantis suggests that at least one clonidine derivative can be used in the composition. There is no specific disclosure of a composition that comprises more than one therapeutic agent. But, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the composition with more than one clonidine derivative in light of the suggestion by DeSantis. One having ordinary skill in the art would have been motivated to include at least two clonidine derivatives with the expectation of obtaining synergistic effect from the clonidine derivatives.

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Uehara et al. In JP 11-130656 discloses a composition comprising fatty acid and

alpha adrenergic inhibitor (English abstract). Clonidine, an alpha-2-adrenergic agonists is an alpha adrenergic inhibitor (see paragraph 43 of US 2005/0191245 as a teaching reference).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 3:30 p.m. (Monday to Friday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Blessing Fubara
Patent Examiner
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